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- Declaration under Rule 4.17:**
— of inventorship (Rule 4.17(iv)) for US only
- Published:**
— without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MODULATED EXCITATION FLUORESCENCE ANALYSIS

(57) Abstract: Fluorescence spectroscopy is used to analyze small numbers of molecules that are present in a relatively small detection volume or zone. Information regarding physical and chemical properties of these molecules is determined by rapidly modulating the wavelength, intensity and/or polarization of laser energy to excite fluorophores that are attached either to the molecule of interest or a molecule that interacts with the molecule of interest. The emission profile of the fluorophores is used to determine useful information about the labeled and/or non-labeled molecules including molecular interactions between the molecules.

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MODULATED EXCITATION FLUORESCENCE ANALYSIS

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] The present invention relates generally to analytical methods where fluorescence spectroscopy is used to analyze small numbers of molecules that are present in a relatively small detection volume or zone. More particularly, the present invention involves determining a wide variety of physical and chemical properties of one or more molecules by rapidly modulating the wavelength, intensity and/or polarization of beams of laser energy to excite fluorophores that are attached either to the molecule of interest or a molecule that interacts with the molecule of interest. The emission profile of the fluorophore is used to determine useful information about various properties of the labeled and/or non-labeled molecules including molecular interactions between the molecules

2. Description of Related Art

[0002] The publications and other reference materials referred to herein to describe the background of the invention and to provide additional detail regarding its practice are hereby incorporated by reference. For convenience, the reference materials are numerically referenced and grouped in the appended bibliography. The contents of these publications and other reference materials are hereby incorporated by reference.

[0003] Understanding the intricate network of interactions occurring in cells allows probing of the mechanisms that control cell growth, maintenance and disease/death. Such interactions include protein-protein, protein-DNA, nucleic acid-nucleic acid, antibody-antigen, receptor-ligand, protein-drug and aggregation-inducing protein-protein interactions. Rapid, reliable and inexpensive methods that can characterize the multitude of the existing interactions is a core technology for proteomics, the scientific domain associated with the mapping of the complement of pair-wise protein-protein interactions on an organism-wide basis. Such interaction maps are necessary for the deciphering of the cell circuitry. Proteomic technologies are a prerequisite for interpreting, utilizing and leveraging the plethora of the genomic

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/19709

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 21/64

US CL : 356/317

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 356/317, 318, 417; 250/458.1, 459.1, 461.1, 461.2; 436/172

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,784,157 A (GORFINKEL et al.) 21 July 1998 (21.07.1998), see the entire document.	1-38

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/19709

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.